L14 ANSWER 9 OF 11 MEDLINE DUPLICATE 6
AN 89098886 MEDLINE
DN 89098886
TI Mapping to molecular resolution in the T to H-2 region of the mouse genome
with a nested set of meiotic recombinants.
AU King T R; Dove W F; Herrmann B; Moser A R; **Shedlovsky A**
CS Laboratory of Genetics, University of Wisconsin-Madison 53706.
NC CA 23076 (NCI)
CA 07175 (NCI)
GM 07133 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Jan) 86 (1) 222-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198904
AB We describe a meiotic fine-structure mapping strategy for achieving molecular access to developmental mutations in the mouse. The induction of lethal point mutations with the potent germ-line **mutagen** N-ethyl-N-nitrosourea has been reported. One lethal mutation of prime interest is an allele at the quaking locus on chromosome 17. To map this mutation, quaking(lethal-1), we have intercrossed hybrid mice that carry distinct alleles at many classical and DNA marker loci on proximal chromosome 17. From this cross we have obtained 337 animals recombinant in the T to H-2 region. This number of crossovers provides a mapping resolution in the size range of single mammalian genes if recombinational hot spots are absent. DNA samples obtained from these recombinant animals can be used retrospectively to map any restriction fragment length polymorphism in the region. This set of DNA samples has been used to map the molecular marker D17RP17 just distal of quaking(lethal-1). With the nested set of crossover DNA samples and appropriate cloning techniques, this tightly linked marker can be used to clone the quaking locus.

L14 ANSWER 4 OF 11 MEDLINE DUPLICATE 2
AN 97224576 MEDLINE
DN 97224576
TI A candidate mouse model for Hartnup disorder deficient in neutral amino acid transport.
AU Symula D J; **Shedlovsky A**; Guillery E N; Dove W F
CS McArdle Laboratory for Cancer Research, University of Wisconsin, Madison 53706, USA.
NC GMO7133 (NIDDK)
DK40393
SO MAMMALIAN GENOME, (1997 Feb) 8 (2) 102-7.
Journal code: BES. ISSN: 0938-8990.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707
EW 19970704
AB The mutant mouse strain HPH2 (hyperphenylalaninemia) was isolated after N-ethyl-N-nitrosourea (ENU) **mutagenesis** on the basis of delayed plasma clearance of an injected load of phenylalanine. Animals homozygous for the recessive hph2 mutation excrete elevated concentrations of many of the neutral amino acids in the urine, while plasma concentrations of these amino acids are normal. In contrast, mutant homozygotes excrete normal levels of glucose and phosphorus. These data suggest an amino acid transport defect in the mutant, confirmed in a small reduction in normalized values of 14C-labeled glutamine uptake by kidney cortex brush border membrane vesicles (BBMV). The hyperaminoaciduria pattern is very similar to that of Hartnup Disorder cases also show niacin deficiency symptoms, of Hartnup Disorder cases also show niacin deficiency symptoms, which are thought to be multifactorially determined. Similarly, the HPH2 mouse exhibits a niacin-reversible syndrome that is modified by diet and by genetic background. Thus, HPH2 provides a candidate mouse model for the study of Hartnup Disorder, an amino acid transport deficiency and a multifactorial disease in the human.

L3 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
AN 1997:42781 BIOSIS
DN PREV199799334769
TI Genetic evaluation of candidate genes for the Mom1 modifier of intestinal neoplasia in mice.
AU Gould, Karen A.; Luongo, Cindy; Moser, Amy R.; McNeley, Melanie K.; Borenstein, Natalie; Shedlovsky, Alexandra; **Dove, William F. (1)** ; Hong, Karen; Dietrich, William F.; Lander, Eric S.
CS (1) 1400 University Ave., Madison, WI 53706 USA
SO Genetics, (1996) Vol. 144, No. 4, pp. 1777-1785.
ISSN: 0016-6731.
DT Article
LA English
AB As genetic mapping of quantitative trait loci (QTL) becomes routine, the challenge is to identify the underlying genes. This paper develops rigorous genetic tests for evaluation of candidate genes for a QTL, involving determination of allelic status in **inbred** strains and fine-structure genetic mapping. For the Mom1 modifier of intestinal adenomas caused by Apc-Min, these tests are used to evaluate two candidate genes: Pla2g2a, a secretory phospholipase, and Rap1GAP, a GTPase activating protein. Rap1GAP passes the first test but is excluded by a single fine-structure recombinant. Pla2g2a passes both tests and is a strong candidate for Mom1. Significantly, we also find that Apc-Min-induced adenomas remain heterozygous for the Mom1 region, consistent with Mom1 acting outside the tumor lineage and encoding a

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS
AN 1992:253207 CAPLUS
DN 116:253207
TI Multiple intestinal neoplasia caused by a mutation in the murine homolog of the APC gene
AU Su, Li Kuo; Kinzler, Kenneth W.; Vogelstein, Bert; Preisinger, Antonette C.; Rapaich Moser, Amy; Luongo, Cindy; Gould, Karen A.; **Dove, William F.**
CS Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21231, USA
SO Science (Washington, D. C., 1883-) (1992), 256(5057), 668-70
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB Germ-line mutations of the APC gene are responsible for familial adenomatous polyposis coli(FAPC), an autosomal dominantly inherited disease in humans. Patients with FAPC develop multiple benign colorectal tumors. Recently, a mouse lineage that exhibits an autosomal dominantly inherited predisposition to multiple intestinal neoplasia (Min) was described. Linkage anal. showed that the murine homolog of the APC gene (mApc) was tightly linked to the Min locus. Sequence comparison of mApc between normal and Min-affected mice identified a nonsense mutation, which co-**segregated** with the Min phenotype. This mutation is analogous to those found in FAPC kindreds and in sporadic colorectal

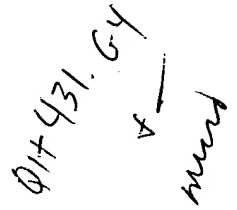
L9 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
AN 1994:256474 BIOSIS
DN PREV199497269474
TI Mutagenesis and mapping of a mouse gene, Clock, essential for circadian behavior.
AU Vitaterna, Martha Hotz; King, David P.; Chang, Anne-Marie; Kornhauser, Jon M.; Lowrey, Philip L.; McDonald, J. David; **Dove, William F.**; Pinto, Lawrence H.; Turek, Fred W.; Takahashi, Joseph S. (1)
CS (1) Natl. Sci. Found. Sci. Technol. Cent., Biol. Timing, Dep. Neurobiol. Physiol., Northwest. Univ., Evanston, IL 60208 USA
SO Science (Washington D C), (1994) Vol. 264, No. 5159, pp. 719-725. ISSN: 0036-8075.
DT Article
LA English
AB In a search for genes that regulate circadian rhythms in mammals, the progeny of mice treated with N-ethyl-N-nitrosourea (ENU) were screened for circadian clock mutations. A semidominant mutation, Clock, that lengthens circadian period and abolishes persistence of rhythmicity was identified. Clock **segregated** as a single gene that mapped to the midportion of mouse chromosome 5, a region syntenic to human chromosome 4. The power of ENU mutagenesis combined with the ability to clone murine genes by map position provides a generally applicable approach to study complex

L11 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1989:129633 CAPLUS
DN 110:129633
TI Mapping to molecular resolution in the T to H-2 region of the mouse genome
with a nested set of meiotic recombinants
AU King, Thomas R.; **Dove, William F.**; Herrmann, Bernhard; Moser, Amy R.; Shedlovsky, Alexandra
CS McArdle Lab. Cancer Res., Univ. Wisconsin, Madison, WI, 53706, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1989), 86(1), 222-6
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB A meiotic fine-structure mapping strategy is described for achieving mol. access to developmental mutations in the mouse. The induction of lethal point mutations with the potent germline **mutagen** N-ethyl-N-nitrosourea has been reported. One lethal mutation of prime interest is an allele at the quaking locus on chromosome 17. To map this mutation, quakinglethal-1, hybrid mice were intercrossed that carry distinct alleles at many classical and DNA marker loci on proximal chromosome 17. From this cross, 337 animals recombinant in the T to H-2 region were obtained. This no. of crossovers provides a mapping resoln. in the size range of single mammalian genes if recombinational hot spots are absent. DNA samples obtained from these recombinant animals can be used retrospectively to map any restriction fragment length polymorphism in the region. This set of DNA samples has been used to map the mol. marker D17Rp17 just distal of quakinglethal-1. With the nested set of crossover DNA samples and appropriate cloning techniques, this tightly

L11 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1991:533377 CAPLUS
DN 115:133377
TI The use of N-ethyl-N-nitrosourea to produce mouse models for human phenylketonuria and hyperphenylalaninemia
AU McDonald, J. David; Bode, Vernon C.; **Dove, William F.**; Shedlovsky, Alexandra
CS Med. Sch., Univ. Wisconsin, Madison, WI, 53706, USA
SO Prog. Clin. Biol. Res. (1990), 340C(Mutat. Environ., Pt. C), 407-13
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal
LA English
AB The isolation and characterization of lab. mice chem. **mutagenized** with N-ethyl-N-nitrosourea to serve as models for human phenylketonuria and hyperphenylalaninemia is discussed.

L11 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1990:196152 CAPLUS
DN 112:196152
TI Pahhph-5: a mouse mutant deficient in phenylalanine hydroxylase
AU McDonald, J. David; Bode, Vernon C.; **Dove, William F.**; Shedlovsky, Alexandra
CS McArdle Lab., Univ. Wisconsin, Madison, WI, 53706, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1990), 87(5), 1965-7
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Mutant mice exhibiting heritable hyperphenylalaninemia have been isolated after ethylnitrosourea **mutagenesis** of the germ line. One mutant pedigree is described in which phenylalanine hydroxylase activity is severely deficient in homozgotes and reduced in heterozygotes while other biochem. components of phenylalanine catabolism are normal. In homozygotes, injection of phenylalanine causes severe hyperphenylalaninemia and urinary excretion of phenylketones but not hypertyrosinemia. Severe chronic hyperphenylalaninemia can be produced when mutant homozygotes are given phenylalanine in their drinking water. Genetic mapping has localized the mutation to murine chromosome 10 at or near the Pah locus, the structural gene for phenylalanine hydroxylase. This mutant provides a useful genetic animal model affected in the same enzyme as in human phenylketonuria.

L11 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 6
AN 1993:409803 BIOSIS
DN PREV199396075528
TI Mouse models of human phenylketonuria.
AU Shedlovsky, Alexandra J. (1); McDonald, J. David; Symula, Derek (1); **Dove, William F. (1)**
CS (1) McArdle Lab. Cancer Res. Lab. Genetics, Univ. Wisconsin, Madison, WI 53706
SO Genetics, (1993) Vol. 134, No. 4, pp. 1205-1210.
ISSN: 0016-6731.
DT Article
LA English
AB Phenylketonuria (PKU) results from a deficiency in phenylalanine hydroxylase, the enzyme catalyzing the conversion of phenylalanine (PHE) to tyrosine. Although this inborn error of metabolism was among the first in humans to be understood biochemically and genetically, little is known of the mechanism(s) involved in the pathology of PKU. We have combined mouse germline **mutagenesis** with screens for hyperphenylalaninemia to isolate three mutants deficient in phenylalanine hydroxylase (PAH) activity and cross-reactive protein. Two of these have reduced PAH mRNA and display characteristics of untreated human PKU patients. A low PHE diet partially reverses these abnormalities. Our success in using high frequency random germline point **mutagenesis** to obtain appropriate disease models illustrates how such **mutagenesis** can complement the emergent power of targeted **mutagenesis** in the mouse. The mutants now can be used as models in



L11 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 5
AN 1994:256474 BIOSIS
DN PREV199497269474
TI **Mutagenesis** and mapping of a mouse gene, Clock, essential for circadian behavior.
AU Vitaterna, Martha Hotz; King, David P.; Chang, Anne-Marie; Kornhauser, Jon M.; Lowrey, Philip L.; McDonald, J. David; **Dove, William F.**; Pinto, Lawrence H.; Turek, Fred W.; Takahashi, Joseph S. (1)
CS (1) Natl. Sci. Found. Sci. Technol. Cent., Biol. Timing, Dep. Neurobiol. Physiol., Northwest. Univ., Evanston, IL 60208 USA
SO Science (Washington D C), (1994) Vol. 264, No. 5159, pp. 719-725. ISSN: 0036-8075.
DT Article
LA English
AB In a search for genes that regulate circadian rhythms in mammals, the progeny of mice treated with N-ethyl-N-nitrosourea (ENU) were screened for circadian clock mutations. A semidominant mutation, Clock, that lengthens circadian period and abolishes persistence of rhythmicity was identified. Clock segregated as a single gene that mapped to the midportion of mouse chromosome 5, a region syntenic to human chromosome 4. The power of ENU **mutagenesis** combined with the ability to clone murine genes by map position provides a generally applicable approach to study complex

L11 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1997:282813 CAPLUS
DN 126:315522
TI Manipulation of the mouse germline in the study of Min-induced neoplasia
AU Bilger, Andrea; Shoemaker, Alex R.; Gould, Karen A.; **Dove, William F.**
CS McArdle Laboratory for Cancer Research, University of Wisconsin Medical School, Madison, WI, 53706, USA
SO Semin. Cancer Biol. (1996), 7(5), 249-260
CODEN: SECBE7; ISSN: 1044-579X
PB Academic
DT Journal; General Review
LA English
AB A review with 118 refs. The Min mouse, generated by random germline **mutagenesis**, carries a mutation in the mouse homolog of APC and is a model of inherited human intestinal tumorigenesis. To identify other genes in the pathway(s) of intestinal tumorigenesis, genes that modify the Min phenotype have been sought. Several have been identified, including Mom1 and the genes for the 5-cytosine DNA methyltransferase and the DNA mismatch repair factor Msh2. Min-dependent tumorigenesis also occurs in mammary glands, the pancreas, and the body wall. The Min mouse has therefore become a model for tumorigenesis in a variety of organs. Identifying modifiers of its phenotype will help in piecing together the

RC261.53

L11 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 4
AN 1997:344677 BIOSIS
DN PREV199799643880
TI The mouse clock mutation behaves as an antimorph and maps within the W-19H
deletion, distal of kit.
AU King, David P.; Vitaterna, Martha Hotz; Chang, Anne-Marie; **Dove, William F.**; Pinto, Lawrence H.; Turek, Fred W.; Takahashi, Joseph S. (1)
CS (1) Dep. Neurobiol. Physiol., Northwestern Univ., 2153 North Campus Dr., Evanston, IL 60208-3520 USA
SO Genetics, (1997) Vol. 146, No. 3, pp. 1049-1060.
ISSN: 0016-6731.
DT Article
LA English
AB Clock is a semidominant mutation identified from an N-ethyl-N-nitrosourea **mutagenesis** screen in mice. Mice carrying the Clock mutation exhibit abnormalities of circadian behavior, including lengthening of endogenous period and loss of rhythmicity. To identify the gene affected by this mutation, we have generated a high-resolution genetic map ( gt 1800 meioses) of the Clock locus. We report that Clock is 0.7 cM distal of
Kit on mouse chromosome 5. Mapping shows that Clock lies within the W-19H deletion. Complementation analysis of different Clock and W-19H compound genotypes indicates that the Clock mutation behaves as an antimorph. This antimorphic behavior of Clock strongly argues that Clock defines a gene centrally involved in the mammalian circadian system.

QH431.G4 + mice

L11 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 3
AN 1998:450363 BIOSIS
DN PREV199800450363
TI A resistant genetic background leading to incomplete penetrance of intestinal neoplasia and reduced loss of heterozygosity in ApcMin/+ mice.
AU Shoemaker, Alex R.; Moser, Amy R.; Midgley, Carol A.; Clipson, Linda; Newton, Michael A.; **Dove, William F. (1)**
CS (1) McArdle Lab. Cancer Res., Univ. Wisconsin, 1400 University Ave., Madison, WI 53706 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (Sept. 1, 1998) Vol. 95, No. 18, pp. 10826-10831. ISSN: 0027-8424.
DT Article
LA English
AB Previous studies of Min/+ (multiple intestinal neoplasia) mice on a sensitive genetic background, C57BL/6 (B6), showed that adenomas have lost heterozygosity for the germ-line ApcMin mutation in the Apc (adenomatous polyposis coli) gene. We now report that on a strongly resistant genetic background, AKR/J (AKR), Min-induced adenoma multiplicity is reduced by about two orders of magnitude compared with that observed on the B6 background. Somatic treatment with a strong **mutagen** increases tumor number in AKR Min/+ mice in an age-dependent manner, similar to results previously reported for B6 Min/+ mice. Immunohistochemical analyses indicate that Apc expression is suppressed in all intestinal tumors from both untreated and treated AKR Min/+ mice. However, the mechanism of Apc inactivation in AKR Min/+ mice often differs from that observed for B6 Min/+ mice. Although loss of heterozygosity is observed in some tumors, a significant percentage of tumors showed neither loss of heterozygosity nor Apc truncation mutations. These results extend our understanding of the effects of genetic background on Min-induced tumorigenesis in several ways. First, the AKR strain carries modifiers of Min in addition to Mom1. This combination of AKR modifiers can almost completely suppress spontaneous intestinal tumorigenesis associated with the Min mutation. Second, even on such a highly resistant genetic background, tumor formation continues to involve an absence of Apc function. The means by which Apc function is inactivated is affected by genetic background. Possible scenarios are discussed.

L11 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
AN 1999:88633 BIOSIS
DN PREV199900088633
TI An action plan for mouse genomics.
AU Battey, James (1); Jordan, Elke; Cox, David; **Dove, William**
CS (1) Natl. Inst. Deafness Other Commun. Disorders, NIH, Build. 31, 9000 Rockville Pike, Bethesda, MD 20892 USA
SO Nature Genetics, (Jan., 1999) Vol. 21, No. 1, pp. 73-75.
ISSN: 1061-4036.
DT Article
LA English
AB The mouse has become the leading animal model for studying biological processes in mammals. Creation of additional genomic and genetic resources will make the mouse an even more useful model for the research community. On the basis of recommendations from the scientific community, the National Institutes of Health (NIH) plans to support grants to generate a 'working draft' sequence of the mouse genome by 2003, systematic **mutagenesis** and phenotyping centres, repositories for mouse strain maintenance, distribution and cryopreservation and training fellowships in